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EXAMINER	
GANGLE, BRIAN J	

ART UNIT	PAPER NUMBER
1645	

DATE MAILED: 08/07/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/532,055	MATTSBY-BALTZER ET AL.	
	Examiner	Art Unit	
	Brian J. Gangle	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 June 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *21-39* is/are pending in the application.

4a) Of the above claim(s) *21-23,27,29 and 34-36* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *24-26,28,30-33 and 37-39* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *21 April 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *4/21/2005*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 21-39 are pending. Claims 21-23, 27, 29, and 34-36 are withdrawn from consideration as being drawn to non-elected inventions. Claims 24-26, 28, 30-33, and 37-39 are currently under examination.

Election/Restrictions

Applicant's election without traverse of Group II in the response filed 6/1/2006 is acknowledged.

Specification

The use of the trademark HyQ-CCM1 has been noted on page 7 in this application. It should be capitalized wherever it appears and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

It should be noted that the cited occurrence of improper use is only exemplary and applicant should review the specification to correct any other use of trademarks.

Information Disclosure Statement

The information disclosure statement filed 4/21/2005 has been considered. An initialed copy is enclosed.

Claim Objections

Claims 24-26, 28, 30-33, and 37-39 are objected to because of the following informalities:

Claims 24-26, 28, 30-33, and 37-39 are dependent on non-elected claims.

Claims 31 and 32 are substantially duplicates.

Claims 38 and 39 are substantially duplicates.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 24-26, 28, 30-33, and 37-39 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The instant claims are drawn to methods of diagnosis of a fungal infection comprising assaying with at least one antibody that is monoclonal antibody reactive with a β(1-3)- and/or a β(1-3) (1-6)-glucan associated epitope in free form, in cell wall fragments or on an intact cell surface (claims 24-26, 28, and 33); wherein said glucan associated epitope is available in cell wall fragments of *C. albicans* and/or *C. neoformans*, or on the cell surface of *C. albicans*, *C. parapsilosis, C. krusei, C. glabrata* and/or *C. neoformans* (claims 30 and 37); wherein said antibody is A10A (claims 31-32 and 38-39).

The courts have recently decided in Randolph J. Noelle v Seth Lederman, Leonard Chess and Michael J. Yellin (CAFC, 02-1187, 1/20/2004) that a patentee of a biotechnological invention cannot necessarily claim a genus after only describing a limited number of species because there may be unpredictability in the results obtained from species other than those specifically enumerated. See Enzo Biochem II, 323 F.3d at 965; Regents, 119 F.3d at 1568. Therefore, based on our past precedent, as long as an applicant has disclosed a "fully characterized antigen," either by its structure, formula, chemical name, or physical properties, or by depositing the protein in a public depository, the applicant can then claim an antibody by its binding affinity to that described antigen. Noelle did not provide sufficient support for the claims to the human CD40CR antibody in his '480 application because Noelle failed to disclose the structural elements of human CD40CR antibody or antigen in his earlier '799 application.

Noelle argues that because antibodies are defined by their binding affinity to antigens, not their physical structure, he sufficiently described human CD40CR antibody by stating that it binds to human CD40CR antigen. Noelle cites Enzo Biochem II for this proposition. This argument fails, however, because Noelle did not sufficiently describe the human CD40CR antigen at the time of the filing of the '799 patent application. In fact, Noelle only described the mouse antigen when he claimed the mouse, human, and genus forms of CD40CR antibodies by citing to the ATCC number of the hybridoma secreting the mouse CD40CR antibody. If Noelle had sufficiently described the human form of CD40CR antigen, he could have claimed its antibody by simply stating its binding affinity for the "fully characterized" antigen. Noelle did not describe human CD40CR antigen. Therefore, Noelle attempted to define an unknown by its binding affinity to another unknown. As a result, Noelle's claims to human forms of CD40CR antibody found in his '480 application cannot gain the benefit of the earlier filing date of his '799 patent application.

In the instant application, applicant has failed to "fully characterize" the antigen (i.e. β(1,3)- and/or β(1,3)(1,6)-glucan associated epitopes) to which the claimed antibody binds. The instant claims are drawn to all monoclonal antibodies with specificity to any β(1,3)- and/or β(1,3)(1,6)-glucan associated epitope. With no definition of "associated" in the specification, a glucan-associated epitope could be taken as any epitope found in a cell wall, or found anywhere within a fungal cell (since glucans are part of fungal cells), or even any epitope associated with many plant cells (since glucans are also part of plant cells). Further, even if one were to limit the epitope to β(1,3)- and/or β(1,3)(1,6)-glucans, these polysaccharides are found in numerous plants and species of fungi, thus one would be unable to differentiate between plant species and particular fungal species. The specification is silent regarding what epitopes would allow one to differentiate between species.

"A10A" refers to a laboratory designation for a monoclonal antibody. Said designation does not provide any structural or functional limitations. Moreover, there is no description in the application of the structure of said antibody. Consequently, since applicant has not fully characterized the antigen to which the claimed antibodies bind, the written description requirements under 35 U.S.C 112, first paragraph have not been met.

The specification does not describe, with any degree of specificity, the β(1,3)- and/or β(1,3)(1,6)-glucan associated epitopes to which the members of the claimed genus of antibodies must bind in order to achieve the desired immunological response, such that the specification might reasonably convey to the skilled artisan that applicant had possession of the claimed invention at the time the application was filed. Nor has applicant described, with any degree of specificity, the claimed antibodies themselves.

MPEP § 2163.02 states, "[a]n objective standard for determining compliance with the written description requirement is, 'does the description clearly allow persons of ordinary skill in the art to recognize that he or she invented what is claimed' ". The courts have decided:

> The purpose of the "written description" requirement is broader than to merely explain how to "make and use"; the applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the "written description" inquiry, whatever is now claimed.

See *Vas-Cath, Inc. v. Mahurkar*, 935 F.2d 1555, 1563-64, 19 USPQ2d 1111, 1117 (Federal Circuit, 1991). Furthermore, the written description provision of 35 USC § 112 is severable from its enablement provision; and adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. See *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (CAFC 1993) and *Amgen Inc. V. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

The Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112, paragraph 1, ``Written Description" Requirement (66 FR 1099-1111, January 5, 2001) state, "[p]ossession may be shown in a variety of ways including description of an actual reduction to practice, or by showing the invention was 'ready for patenting' such as by disclosure of drawings or structural chemical formulas that show that the invention was complete, or by describing distinguishing identifying characteristics sufficient to show that the applicant was in possession of the claimed invention" (Id. at 1104). Moreover, because the claims encompass a genus of variant species, an adequate written description of the claimed invention must include sufficient description of at least a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics sufficient to show that applicant was in possession of the claimed genus. However, factual evidence of an actual

reduction to practice has not been disclosed by applicant in the specification; nor has applicant shown the invention was "ready for patenting" by disclosure of drawings or structural chemical formulas that show that the invention was complete; nor has applicant described distinguishing identifying characteristics sufficient to show that applicant were in possession of the claimed invention at the time the application was filed.

As evidenced by Greenspan et al. (Nature Biotechnology 17: 936-937, 1999), defining epitopes is not as easy as it seems. Greenspan et al. recommends defining an epitope by the structural characterization of the molecular interface between the antigen and the antibody is necessary to define an "epitope" (page 937, column 2). According to Greenspan et al., an epitope will include residues that make contacts with a ligand, here the antibody, but are energetically neutral, or even destabilizing to binding. Furthermore, an epitope will not include any residue not contacted by the antibody, even though substitution of such a residue might profoundly affect binding. Accordingly, it follows the epitope to which any given antibody binds can only be identified empirically. Even using a competition assay, the skilled artisan cannot determine whether an antibody binds the same epitope as another antibody because an antibody that competes with another does not necessarily bind the same epitope as the other; rather, one antibody may bind a spatially overlapping epitope to sterically hinder binding of the other. Therefore, absent a detailed and particular description of a representative number, or at least a substantial number of the members of the genus of epitopes to which the members of the claimed genus of antibodies must bind, the skilled artisan could not immediately recognize or distinguish members of the claimed genus of antibodies. Moreover, since the specification has not identified which amino acids of the genus of epitopes to which the members of the claimed genus of antibodies must bind, which are critical or essential to the binding, one skilled in the art would not recognize that applicant had possession of the claimed invention at the time the application was filed.

Claims 31-32 and 38-39 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

It is apparent that the monoclonal antibody represented by the designation A10A is required in order to practice the invention. Specifically, it is noted that claims 31-32 and 38-39 recite deposited material. The deposit of biological organisms is considered by the Examiner to be necessary for the enablement of the current invention (see 37 CRF 1.808(a)).

If the deposit is made under terms of the Budapest Treaty, then an affidavit or declaration by Applicants or person(s) associated with the patent owner (assignee) who is in a position to make such assurances, or a statement by an attorney of record over his or her signature, stating that the deposit has been made under the terms of the Budapest Treaty *and* that all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon the granting of a patent, would satisfy the deposit requirements. See 37 CFR 1.808.

If a deposit is not made under the terms of the Budapest Treaty, then an affidavit, or declaration by Applicants or person(s) associated with the patent owner (assignee) who is in a position to make such assurances, or a statement by an attorney of record over his or her signature, stating that the following criteria have been met:

1) during the pendency of the application, access to the deposit will be afforded to one determined by the Commissioner to be entitled thereto;

2) all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon the granting of a patent; and

3) the deposits will be maintained for a term of at least thirty (30) years from the date of the deposit or for the enforceable life of the patent or for a period of at least five (5) years after the most recent request for the furnishing of a sample of the deposited material, whichever is longest; and

4) a viability statement in accordance with the provisions of 37 CFR 1.807; and

5) the deposit will be replaced should it become necessary due to inviability, contamination or loss of capability to function in the manner described in the specification.

In addition, the identifying information set forth in 37 CRF 1.809(d) should be added to the specification. See 37 CFR 1.803 - 1.809 for additional explanation of these requirements.

Claims 24-26, 28, 30-33, and 37-39 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention without undue experimentation.

Undue experimentation is a conclusion reached by weighing the noted factual considerations set forth below as seen in *In re* Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988). A conclusion of lack of enablement means that, based on the evidence regarding each of the factors below, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the claimed invention without undue experimentation.

Nature of the invention: The instant claims are drawn to methods for the diagnosis of a fungal infection comprising assaying with at least one antibody wherein said antibody is a monoclonal antibody reactive with a β(1-3)- and/or a β(1-3) (1-6)-glucan associated epitope in free form, in cell wall fragments or on an intact cell surface (claims 24-26, 28, and 33); wherein said glucan associated epitope is available in cell wall fragments of *C. albicans* and/or *C. neoformans*, or on the cell surface of *C. albicans*, *C. parapsilosis, C. krusei, C. glabrata* and/or *C. neoformans* (claims 30 and 37); wherein said antibody is A10A (claims 31-32 and 38-39). Claims 28 and 37-39 further recite the limitation that the presence of β(1,3)-glucans indicates a fungal infection in the patient. Claims 26 and 33 require that the diagnosis be performed on mucosal secretions or urine, and claim 25 is drawn to said method where the method is used to diagnose Candida vaginitis or mucocutane candidiasis.

Breadth of the claims: The instant claims are drawn to all monoclonal antibodies with specificity to any β(1,3)- and/or β(1,3)(1,6)-glucan associated epitope. With no definition of "associated" in the specification, a glucan-associated epitope could be taken as any epitope found in a cell wall, or found anywhere within a fungal cell (since glucans are part of fungal cells), or even any epitope associated with many plant cells (since glucans are also part of plant cells). With the exception of claims 25 and its dependent claim 26, the claims are drawn to methods of diagnosing all fungal infections of all types. This would include every species of fungus capable of causing infection, and it would include mycoses of all types, including systemic, epidermal,

nail, and gastrointestinal infections. With the exception of claims 26 and 33, all samples, including non-biological samples, are encompassed by the claims. The claims encompass antibodies directed to β(1-3)- and/or a β(1-3) (1-6)-glucan associated epitopes from all organisms, and, as there is no definition of "associated," the claims also encompass epitopes from all fungal antigens, as well as epitopes from all plant cell antigens. As the term infection can be applied to environmental samples, claims 24 and 30-32 are not even limited to fungal infections in animals.

Working Examples/Guidance of Specification: The specification fails to describe immunoepitopes against which the claimed antibodies are raised and must subsequently bind. The working examples disclose specific antibodies that meet the limitations of the instant claims. However, these "examples" refer to antibodies by their laboratory designations which are not sufficient to provide enablement for the full scope of the rejected claims. The specification is silent as to what specific "immunoepitope" meets the limitations of the claims. Additionally, the specification is silent with regard to what epitopes are cross-reactive and what epitopes would allow one to differentiate between species. There is no showing in the specification that either A10A, or any other antibodies can be used to detect infection using any type of sample. The only information regarding A10A or other antibodies is that they are capable of binding β(1-3)- and/or a β(1-3) (1-6)-glucans. The specification states that β(1,3)-glucan has been found in the serum of all patients with candidemia, but in none of women with superficial Candida infection, or in healthy controls (page 14). The specification further states that "the presence of β(1,3)-glucans in the serum of patients with deep fungal infections may be a useful marker for laboratory diagnosis of these infections. Future investigations will address the usefulness of our mAbs to glucan in an immunoassay-based kit for the rapid detection of β(1,3)-glucans in blood samples, in other specimens from patients with invasive fungal infections, or in other body fluids such as mucosal secretions and urine." All guidance regarding the claimed method is prophetic.

State of the prior art and Unpredictability of the art: In the instant application, applicant has failed to "fully characterize" the antigen (i.e. β(1,3)- and/or β(1,3)(1,6)-glucan associated epitopes) to which the claimed antibody binds. The instant claims are drawn to methods utilizing all antibodies with specificity to any β(1,3)- and/or β(1,3)(1,6)-glucan associated epitopes. Consequently, since applicant has not fully characterized the antigen to

which the claimed antibodies bind, hence the skilled artisan would not be able to make the claimed invention.

While the skill in the art of immunology is high, to date, prediction of a specific immune response for any given composition in any given animal is quite unpredictable. Moreover, protein chemistry is probably one of the most unpredictable areas of biotechnology. Consequently, the effects of sequence dissimilarities upon protein structure and function cannot be predicted. Bowie et al (Science, 1990, 247:1306-1310) teach that an amino acid sequence encodes a message that determines the shape and function of a protein and that it is the ability of these proteins to fold into unique three-dimensional structures that allows them to function, carry out the instructions of the genome and form immunoepitopes. Bowie et al. further teach that the problem of predicting protein structure from sequence data and in turn utilizing predicted structural determinations to ascertain functional aspects of the protein is extremely complex. (column 1, page 1306). Bowie et al further teach that while it is known that many amino acid substitutions are possible in any given protein, the position within the protein's sequence where such amino acid substitutions can be made with a reasonable expectation of maintaining function are limited. Certain positions in the sequence are critical to the three dimensional structure/function relationship and these regions can tolerate only conservative substitutions or no substitutions (column 2, page 1306). Additionally, Greenspan et al. (Nature Biotechnology 17: 936-937, 1999), disclose defining epitopes is not as easy as it seems. Greenspan et al. recommends defining an epitope by the structural characterization of the molecular interface between the antigen and the antibody is necessary to define an "epitope" (page 937, column 2). According to Greenspan et al., an epitope will include residues that make contacts with a ligand, here the antibody, but are energetically neutral, or even destabilizing to binding. Furthermore, an epitope will not include any residue not contacted by the antibody, even though substitution of such a residue might profoundly affect binding. Accordingly, it follows that the immunoepitopes that can elicit a particular immune response (i.e. generation of an antibody that bind to a given epitope) can only be identified empirically. This constitutes undue experimentation. Therefore, given the lack of success in the art, the lack of working examples commensurate in scope to the claimed invention and the unpredictability of the generation of a specific immune response, the

specification does not enable any person of skill in the art to which it pertains, or with which it is most nearly connected, to make and use the claimed invention.

With regard to methods of diagnosing fungal infections, monoclonal antibodies capable of binding to β(1,3)-glucans have been shown in the art, and assays exist for determining the presence of β(1,3)-glucans in environmental samples, as well as serum samples. Tamura et al. (J. Clin. Lab. Anal., 11:104-109, 1997) disclose an assay to detect Candida β(1,3)-glucans in murine serum samples (see Results). Milton et al. (Appl. Environ. Microbiol., 67:5420-5424, 2001) present an ELISA to determine the presence of β(1,3)-glucans in environmental samples (see whole article). However, these studies have shown an ability to detect β(1,3)-glucans, not to diagnose infection, or to determine the presence of fungal cells, especially in specific areas of the body. Tamura only studied serum samples, and in these did not show a statistically valid correlation between fungal cells and β(1,3)-glucans. Using methods other than antibody detection, Odabasi et al. (Clin. Infect. Dis., 39:199-205, 2004) found serum samples that were positive for β(1,3)-glucans in patients with no known fungal infections, and found serum samples that were negative for β(1,3)-glucans in patients that likely had fungal infections (see page 204, column 1, paragraph 3 – column 2, paragraph 2; see also, table 2). Murray et al. (Medical Microbiology, 4th ed., 2002) state that Candida species can be isolated from healthy mucosal surfaces of the oral cavity, vagina, gastrointestinal tract, and rectal area. As many as 80% of people may show colonization of these sites in the absence of disease (see page 664, column 2, paragraph 3).

Therefore, while monoclonal antibodies may be used to detect the presence and the amount of β(1,3)-glucans present in a sample (environmental, serum, culture, etc.), this is not correlated with infection. Applicants have not shown the method to be effective, and only prophetically discuss said method. Applicants stated that in patients with superficial infection, no β(1,3)-glucans were found in serum. This is in agreement with the art that shows that β(1,3)-glucans were not detected in some infected patients. The skilled artisan would expect that urine samples would not be predictive of dermatophytic infections, and that oral samples would not be predictive of vaginal infections. Further, one would be unable to distinguish between Candida vaginitis or mucocutane candidiasis and the normal colonization that is found in 80% of the population using said method. Moreover, the epitopes to which the claimed antibodies must bind

are present in many species. One would be unable to distinguish between these species using the claimed methods, and since said epitopes can be found on plant cells, one could not even determine if the β(1,3)-glucans were fungal in origin.

Therefore, in view of the lack of guidance in the specification and the art, the specification does not enable one of skill in the art to use the invention as claimed.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 24-26, 28, 30-33, and 37-39 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The claims contain no active steps other than "assaying." It is not clear what active method steps are involved in "assaying," nor is it clear what is being assayed.

Claims 24-26, 28, 30-33, and 37-39 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 25 is rendered vague and indefinite by the phrase "wherein said fungal infection is Candida vaginitis or mucocutane candidiasis." Candida vaginitis is a disease caused by a fungal infection, it is not the infection itself. In addition, mucocutane candidiasis is a heterogeneous disorder of the immune system that is characterized by persistent Candida infections of the mucous membranes. As with Candida vaginitis, mucocutane candidiasis is a disease caused by a fungal infection, and it is not the fungal infection itself.

Claim 26 is rendered vague and indefinite by the phrase "wherein said diagnosis is performed on mucosal secretions or urine." Diagnosis is the determination of the nature of a disease; therefore, one would not perform a diagnosis on urine or mucosal secretions, as they would not have a disease. A patient would have a disease, such as mucocutane candidiasis, which is caused by a fungal infection, which might be diagnosed by the detection of a fungal infection of the mucous membranes.

Claim 28 recites the limitation "said patient" in line 4. There is insufficient antecedent basis for this limitation in the claim.

Claim 33 is rendered vague and indefinite by the phrase "wherein said diagnosis is performed on mucosal secretions or urine." Diagnosis is the determination of the nature of a disease; therefore, one would not perform a diagnosis on urine or mucosal secretions, as they would not have a disease. A patient would have a disease, such as mucocutane candidiasis, which is caused by a fungal infection, which might be diagnosed by the detection of a fungal infection of the mucous membranes.

Claim 37 recites the limitation "said patient" in line 4. There is insufficient antecedent basis for this limitation in the claim.

Claim 38 recites the limitation "said patient" in line 4. There is insufficient antecedent basis for this limitation in the claim.

Claim 39 recites the limitation "said patient" in line 4. There is insufficient antecedent basis for this limitation in the claim.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 24-26, 30, and 33 are rejected under 35 U.S.C. 102(b) as being anticipated by Brawner *et al.* (J. Clin. Microbiol., 27:1335-1341, 1989).

The instant claims are drawn to a method for the diagnosis of a fungal infection comprising assaying with at least one antibody wherein the antibody is a monoclonal antibody reactive with a β(1-3)- and/or a β(1-3) (1-6)-glucan associated epitope in free form, in cell wall fragments or on an intact cell surface (claim 24); wherein said fungal infection is Candida vaginitis or mucocutane candidiasis (claim 25); wherein said diagnosis is performed on mucosal secretions or urine (claim 26); or where the β(1-3)- and/or β(1-3) (1-6)-glucan associated epitope

is available in cell wall fragments of *C. albicans* and/or *C. neoformans*, or on the cell surface of *C. albicans, C. parapsilosis, C. krusei, C. glabrata* and/or *C. neoformans* (claim 30).

Brawner *et al.* disclose a method of determining the presence of Candida in oral candidiasis, using monoclonal antibodies directed against cell surface antigens composed of mannose and glucose (see abstract and page 1335, column 2, paragraph 1). The epitope to which the antibody binds is a fungal cell surface antigen, and is therefore associated with β-glucans, and is available on the cell surface of *Candida albicans*. Brawner *et al.* used samples obtained from the tongue and buccal epithelium, and would thus contain mucosal secretions (see page 1336, column 1, paragraph 2). With no definition or active steps defining a "diagnosis performed on mucosal secretions," this limitation is being interpreted as an assay of mucosal secretions.

Claims 24, 26, 28, 30, and 37 are rejected under 35 U.S.C. 102(b) as being anticipated by Wakshull *et al.* (PCT Publication WO 99/31510, 6/1999).

The instant claims are drawn to a method for the diagnosis of a fungal infection comprising assaying with at least one antibody wherein the antibody is a monoclonal antibody reactive with a β(1-3)- and/or a β(1-3) (1-6)-glucan associated epitope in free form, in cell wall fragments or on an intact cell surface (claim 24); wherein said diagnosis is performed on mucosal secretions or urine (claim 26); or where the β(1-3)- and/or β(1-3) (1-6)-glucan associated epitope is available in cell wall fragments of *C. albicans* and/or *C. neoformans*, or on the cell surface of *C. albicans, C. parapsilosis, C. krusei, C. glabrata* and/or *C. neoformans* (claim 30). Claims are also drawn to a method for diagnosing fungal infections comprising performing an assay for the detection of β(1,3)-glucans in a sample using a monoclonal antibody reactive with a β(1-3)- and/or a β(1-3) (1-6)-glucan associated epitope in free form, in cell wall fragments or on an intact cell surface, and wherein the presence of β(1,3)-glucans indicates a fungal infection in said patient (claim 28); and wherein the where the β(1-3)- and/or β(1-3) (1-6)-glucan associated epitope is available in cell wall fragments of *C. albicans* and/or *C. neoformans*, or on the cell surface of *C. albicans, C. parapsilosis, C. krusei, C. glabrata* and/or *C. neoformans* (claim 37).

Wakshull *et al.* disclose a method of diagnosis of fungal infection where a sample is obtained from an individual and said sample is assayed, with monoclonal antibodies for the presence of β(1,3)-glucans, which would be indicative of infection (see page 19, lines 1-10 and 19-25). The biological sample can be human urine, and said antibodies can bind to β(1,3)-glucans from *Candida albicans* (see figures 7-8).

Claims 24-26, 30, and 33 are rejected under 35 U.S.C. 102(b) as being anticipated by Bargatze *et al.* (PCT Publication WO 00/48633, 8/2000).

The instant claims are drawn to a method for the diagnosis of a fungal infection comprising assaying with at least one antibody wherein the antibody is a monoclonal antibody reactive with a β(1-3)- and/or a β(1-3) (1-6)-glucan associated epitope in free form, in cell wall fragments or on an intact cell surface (claim 24); wherein said fungal infection is Candida vaginitis or mucocutane candidiasis (claim 25); wherein said diagnosis is performed on mucosal secretions or urine (claims 26 and 33); or where the β(1-3)- and/or β(1-3) (1-6)-glucan associated epitope is available in cell wall fragments of *C. albicans* and/or *C. neoformans*, or on the cell surface of *C. albicans, C. parapsilosis, C. krusei, C. glabrata* and/or *C. neoformans* (claim 30).

Bargatze *et al.* disclose a method to capture *Candida* antigens in the vaginal secretions of a patient (see page 38, lines 14-17). Said method is useful for diagnosing what disease is present and the extent of infection of said disease (see page 23, lines 24-30). Bargatze *et al.* disclose that said disease can be vaginal candidiasis (see page 6, lines 15-24). Said method uses monoclonal antibodies that bind to an epitope of a hydrophobic cell wall protein of *C. albicans* (see page 6, lines 25-28, and page 8, lines 10-15).

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian J. Gangle whose telephone number is (571) 272-1181. The examiner can normally be reached on M-F 8-4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith can be reached on (571) 272-0864. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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7/17/2006

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